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Registration Decision RD2015-15

Difenoconazole

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Registration Decision for Difenoconazole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Difenoconazole Technical Fungicide, Ascernity Fungicide and Instrata II A Fungicide containing the technical grade active ingredients difenoconazole and benzovindiflupyr to control diseases in turf.

Difenoconazole is currently registered in Canada as a seed treatment (the detailed review for this use can be found in the Proposed Regulatory Decision Document PRDD99-01, *Difenoconazole*) and to control or suppress fungal diseases on a variety of fruit and vegetable crops (the detailed review for this use can be found in the Evaluation Report ERC2011-06, *Difenoconazole*).

Difenoconazole is formulated with benzovindiflupyr in the two end use products being proposed for use in turf.

A full review of benzovindiflupyr can be found in PRD2015-07: *Benzovindiflupyr*.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration on turf in the consultation document[1] Proposed Registration Decision PRD2015-10, *Difenoconazole*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for difenoconazole and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2015-10. This decision is consistent with the proposed registration decision stated in PRD2015-10.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2015-10, *Difenoconazole* that contains a detailed evaluation of the information submitted in support of this registration.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is Difenoconozole?

Difenoconazole is a triazole fungicide belonging to the demethylation inhibitor (DMI) group of fungicides (Group 3). Difenoconazole is approved in Canada as a foliar fungicide and a seed treatment on field crops, fruits and vegetables.

Health Considerations

Can Approved Uses of Difenoconazole Affect Human Health?

Difenoconazole is unlikely to affect your health when used according to label directions.

Potential exposure to difenoconazole may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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[3] "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

[4] "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when difenoconazole products are used according to label directions.

In laboratory animals, the technical grade active ingredient difenoconazole was of slight acute toxicity by the oral route; consequently, the hazard signal words "CAUTION – POISON" are required on the Difenoconazole Technical Fungicide label. It was of low acute toxicity dermally and through inhalation exposure. Difenoconazole was mildly irritating to the eyes, minimally irritating to the skin and did not cause an allergic skin reaction. The hazard signal words "CAUTION – EYE IRRITANT" are required on the Difenoconazole Technical Fungicide label.

Ascernity Fungicide and Instrata II A Fungicide containing benzovindiflupyr and difenoconazole was slightly acutely toxic via the oral route and of low acute toxicity via the dermal and inhalation routes. It was moderately irritating to the eyes, but non-irritating to the skin and did not cause an allergic skin reaction. Based on these findings, the signal word and hazard statements "POISON" and "WARNING –EYE IRRITANT" are required on the product label.

There was limited evidence that difenoconazole caused damage to the nervous system or immune system. Difenoconazole did not cause birth defects in animals and there were no effects on the ability to reproduce. There was no evidence to suggest that difenoconazole damaged genetic material. Health effects in animals given repeated doses of difenoconazole included effects on the liver, body weight and food consumption. Difenoconazole caused liver tumours in mice, but not in rats. These tumours were observed at very high doses that were considered excessive.

When difenoconazole was given to pregnant animals, effects of a serious nature were observed on the developing fetus at doses that were toxic to the mother. There was an increased incidence of fetal mortality in utero, while the mothers had severely depressed body weight gains. The risk assessment takes these effects into account in determining the allowable level of human exposure to difenoconazole.

The risk assessment protects against the effects of difenoconazole by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and drinking water are not of health concern.

Chronic dietary intake estimates (food plus drinking water) revealed that the general population and children between the age of one and two years old, the subpopulation which would ingest the most difenoconazole relative to body weight, are expected to be exposed to less than 61% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from difenoconazole is not of health concern for all population subgroups. There are no lifetime cancer risks of concern from the use of difenoconazole.

The acute dietary (food plus drinking water) intake estimate for the population subgroup of women aged between 13 and 49 years old was less than 14% of the acute reference dose. Estimates for all other subpopulations, including the highest exposed subpopulation of children between the age of one and two years old, were also less than 14%. Hence, none are of health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

No metabolism or residue data are required by the PMRA to support the registration of the end-use products Ascernity Fungicide and Instrata II A Fungicide (a component of Instrata II Fungicide Tank-Mix), both for use on golf course turfgrass in Canada.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern when Ascernity Fungicide and Instrata II A Fungicide are used according to the proposed label directions.

Adults and youth may be exposed to difenoconazole while golfing on treated courses. Based on the expected short to intermediate term duration of this activity, risk to golfers is not a concern.

Occupational Risks From Handling Difenoconazole

Occupational risks are not of concern when Ascernity Fungicide and Instrata II A Fungicide are used according to the proposed label directions, which include protective measures.

Golf course workers, who mix, load or apply Ascernity Fungicide or Instrata II A Fungicide, as well as field workers re-entering freshly treated turf can come in direct contact with difenoconazole residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying these products must wear a long-sleeved shirt and long pants, chemical-resistant gloves, and goggles when mixing, loading and applying or during equipment clean-up or repair.

Goggles and chemical-resistant gloves are not required during groundboom application. The label also requires that workers and golfers do not enter treated areas until residues have dried. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk from exposure to difenoconazole for these individuals is not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Difenoconazole Is Introduced Into the Environment?

When used according to label directions, difenoconazole does not pose an unacceptable risk to the environment.

When difenoconazole is used to control fungal diseases on turf, the environmental fate characteristics are similar to those expected when it is used on agricultural food crops. Any difenoconazole deposited on the ground will remain in soil for a considerable period of time as it is broken down very slowly. With repeated yearly applications, difenoconazole will accumulate in soil and could eventually move to lower soil depths. Difenoconazole is not volatile and is not expected to bioaccumulate.

The turf use of difenoconazole poses potential risks to non-target terrestrial organisms including beneficial arthropods and plants. When used near aquatic habitats, it poses potential risks to amphibians, freshwater and marine/estuarine invertebrates, freshwater and marine/estuarine fish, and freshwater algae. To minimize exposure to non-target organisms, spray buffer zones are required to protect terrestrial, freshwater and marine/estuarine habitats adjacent to areas treated with difenoconazole. Toxicity statements are also required on the product label for terrestrial organisms, beneficial, arthropods, plants, freshwater and marine/estuarine invertebrates and fish and fresh water algae.

Value Considerations

What Is the Value of Instrata II Fungicide and Ascernity Fungicide?

Instrata II and Ascernity Fungicides contain multiple active ingredients that are used in combination to control important diseases on turf.

Instrata II Fungicide is a co-pack product consisting of two components for control of pink and grey snow moulds. Component A contains benzovindiflupyr and difenoconazole fungicides and Component B contains fludioxonil fungicide. Ascernity Fungicide contains benzovindiflupyr and difenoconazole fungicides and controls summer diseases.

Managers of high quality turf found on golf courses and sod farms must preserve the functional and aesthetic characteristics of the crop. Golf courses require high levels of control of turf pests to ensure play areas are maintained according to the expectations of members. Difenoconazole demonstrated a contribution to efficacy against important summer and winter diseases. The activity of multiple active ingredients contributes to overall disease control and the management of resistance. The registration of these turf products provides additional tools to help combat fungicide resistance and enhance control of several key pathogens.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Instrata II A Fungicide and Ascernity Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with difenoconazole on the skin or through inhalation of spray mists, anyone mixing/loading and applying Ascernity or Instrata II A Fungicide must wear a long sleeved-shirt and long pants, chemical-resistant gloves, and goggles when mixing, loading and applying or during equipment clean-up or repair. Goggles and chemical-resistant gloves are not required during groundboom application. The label also requires that workers and golfers do not enter treated areas until residues have dried. In addition, a restriction against use in residential areas was added to the label.

Environment

Include all the environmental label statements that were previously identified as required (ERC-2011-06, *Difenoconazole*), as well as spray buffer zones for terrestrial and aquatic habitats that have been updated to reflect use on turf.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2015-10, *Difenoconazole)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.